UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/923,684	08/06/2001	Ramaswamy Narayanan	6818-24	1544

7590 07/25/2003

Gregory A. Nelson, Esq.
Akerman, Senterfitt & Eidson, P.A.
222 Lakeview Avenue, Suite 400
Post Office Box 3188
West Palm Beach, FL 33402-3188

EXAMINER	
MCGARRY, SEAN	
ART UNIT	**PAPER NUMBER**
1635	11

DATE MAILED: 07/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No.	Applicant(s)	
	09/923,684	NARAYANAN, RAMASWAMY	
	Examiner	Art Unit	
	Sean R McGarry	1635	

-- Th MAILING DATE of this communication appears on the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-58* is/are pending in the application.

4a) Of the above claim(s) *1-24 and 31-58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-29* is/are rejected.

7)☒ Claim(s) *30* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *06 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7,8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's election without traverse of Group 25 in Paper No. 10, filed 4/17/03 is acknowledged.

Claims 1-24 and 31-58 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 10.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claims 25-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The invention is drawn to the inhibition of expression of a SIM2 short form gene via an agent that decreases the expression of the SIM2 short form in a cell. The specification discloses SEQ ID NO: 2 which corresponds to the cDNA encoding the human species of SIM2 short form gene. The specification discloses two specific antisense SEQ ID NO: 11 and 12 that inhibit SIM2 expression. SEQ ID NO: 2, and 11

and 12 meet the written description provisions of 35 USC 112, first paragraph. However, the claims are directed to encompass agents that inhibit expression of gene sequences, sequences that hybridize to SEQ ID NO: 2, corresponding sequences from other species, mutated sequences, allelic variants, splice variants, sequences that have a recited degree of identity (similarity, homology), and so forth (see pages 3-5 and 9-11, for example). None of these sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO:2 in the method, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or agnets for inhibition, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack

of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an

adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

The specification fails to describe what features (i.e. structures) of any particular agent would be expected to impart the predictable function of inhibiting a SIM2 of SEQ ID NO: 2 or the various variation of a SIM2 as defined by the specification. The disclosure of a method of screening does not substitute for a description of the invention. One in the art does not know based on the instant specification what agents could be used in the instant invention and further do not know the structure of the scope

of SIM2 genes instantly targeted, for example. It is noted that the instantly claimed invention (claims 25-29) is not even limited to a direct inhibition of a SIM2 but also reads on inhibitors that may indirectly inhibit the expression of SIM2 short form, for example (See context of claim 27 in comparison to claim 28. Claim 28 requires that the antisense oligonucleotide hybridize to a SIM2, which clearly implies that such hybridization is not required in the method of claim 27, for example).

Therefore, only a method comprising the use of SEQ ID NO: 12 (claim 30) to inhibit the expression of SEQ ID NO: 2 but not the full breadth of the claim (or none of the sequences encompassed by the claim) meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 25-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kong et al [FASEEB Journal, Vol. 15(5):A762, 3/08/2001] and Chrast et al [cited by

applicant] in view of Agrawal et al., Molecular Medicine Today, Vol. 6:72-81, February 2000] and Sharma et al., BioEssays Vol. 17:1055-1063, 1995].

The invention is a method of decreasing SIM2 short form gene expression via the introduction of an agent that inhibits the expression of SIM2 short forming a cell (claim 25, where the agent is an oligonucleotide (claim 26) and wherein the oligonucleotide is an antisense oligonucleotide (claim 27) and where the antisense oligonucleotide is at least 18 nucleotides in length (claim 29) and where the antisense oligonucleotide hybridizes to a SIM2 nucleic acid (claim 28).

Kong et al have taught the inhibition of SIM2 via an antisense oligonucleotide in the study of SIM2 function and transcription factors having a PAS-domain. Kong et al do not teach a sequence for the target SIM2 or disclose the sequence of the antisense used.

Chrast et al have taught the sequence for SIM2 (Gen Bank U80457) and discuss its similarity in structure to the Drosophilae single minded gene and provide characterizations such as expression as determined by Northern blots, for example and discuss that these are potentially transcription factors (see page 620, for example). It is stated on page 620 that it is unknown what phenotypes may be associated with SIM2 mutants. It is stated on page 621 that SIM2, with its three copies, is an exceptional candidate to be associated with certain phenotypes.

Sharma et al and Agrawal are relied upon to show that antisense oligonucleotides, in general, are tools used in the art for the determination of gene function and show that antisense can function by hybridizing to its target and show in

table 1 (Agrawal), for example that it is routine to use antisense at least 18 nucleotides in length .

Antisense technology has been effective in blocking the expression of targeted genes and validating drug therapy targets and further has become an essential tool for determining gene function as has been shown by Sharma et al and Agrawal et al in general and has been shown for SIM2 in particular by Kong et al. Chrast et al have provided what was lacking in Kong et al for one in the art to make antisense to a SIM2 target, a sequence. The prior art clearly provides an expectation of success in using antisense in the determination of SIM2 function since Kong et al have demonstrated such. Sharma et al and Agrawal et al have provided general motivation for using antisense for inhibiting a target gene to determine its function and Kong et al have provided specific motivation for antisense inhibition of SIM2 and Chrast et al have provided specific motivation to inhibit SIM2 short form, for example.

The invention as a whole would therefor have been *prima facie* obvious to one in the art at the time the invention was made

Claim 30 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The art made of record and not relied upon is considered pertinent to applicant's disclosure. DeYoung et al., PNAS Vol. 100(8):4760-4765, a post filing reference describes the instantly claimed subject matter.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean R McGarry whose telephone number is (703)305-7028. The examiner can normally be reached on M-Th (6:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SRM
July 22, 2003

SEAN McGARRY
PRIMARY EXAMINER
1635